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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,545	10/11/2007	Benny V. Jensen	HOI-11502/16	2550

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EXAMINER	
KAROL, JODY LYNN	
ART UNIT	PAPER NUMBER
1627	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,545	JENSEN ET AL.	
	Examiner	Art Unit	
	Jody L. Karol	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/28/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/5/2007 and 12/29/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Amendment filed 7/28/2006. Claims 4-20 have been amended. Claims 21-22 have been cancelled. Claims 1-20 are pending and examined on the merits herein.

Priority

1. This Application is a 371 of PCT/DK2005/000065 International Filing Date: 1/28/2005 which claims foreign priority to Application No. PA 2004 00136 filed in Denmark on 1/30/2004 and domestic priority to US Provisional Application No. 60/553,661 filed on 3/16/2004.

Information Disclosure Statement

2. The information disclosure statements (IDS) filed on 2/5/2007 and 12/29/2009 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-20 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cosmetic method for improving aspects of an

individual's skin tone including methods for the treatment of skin aging or wrinkling, comprising administering captopril or ACE enzyme inhibitor dipeptides , does not reasonably provide enablement for a cosmetic method for improving aspects of an individual's skin tone including methods for the treatment of skin aging or wrinkling comprising administering at least one of each and every ACE inhibitor and/or angiotensin II receptor antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without **undue experimentation** *(United States v. Telectronics, Inc.,* 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman,* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art. All of the factors have been considered with regard to the claims, with the most relevant factors discussed below:

(1) The nature of the invention: The instant invention pertains to cosmetic

methods of improving aspects of an individual's skin tone comprising contacting the skin with a composition comprising at least one of any ACE inhibitor and/or angiotensin II receptor antagonist and methods of treatment of skin aging or wrinkling comprising administering any ACE inhibitor and/or angiotensin II receptor antagonist to an individual in need thereof.

(2) The breadth of claims: Claims 1-14 are directed to methods of improving aspects of an individual's skin tone comprising contacting the skin with a composition comprising at least one of any ACE inhibitor and/or angiotensin II receptor antagonist. Claims 15-20 are directed to methods of treatment of skin aging or wrinkling comprising administering any ACE inhibitor and/or angiotensin II receptor antagonist to an individual in need thereof. The improvement of aspect of an individual's skin tone or the treatment of skin aging or wrinkling includes treatment with any ACE inhibitor and/or angiotensin inhibitor. This encompasses treatment with a large number of compounds that may or may not yet be known, which is not supported by the instant specification.

(3) The state of the prior art: It is known in the art to treat the aging or damaged skin with certain ACE inhibitors. For example, Alert et al. teach the treatment of UV-induced skin damage with compositions containing captopril (see US 5,728,373 - cited on IDS). Further, Lintner et al. (teach the treatment of bags and circles under the eyes, visible signs of ageing and fatigue, by administering a composition comprising ACE enzyme inhibitor dipeptides (see US 2005/0142092 A1 - cited on IDS). However, there is no evidence in the prior art that administering ACE inhibitors and/or angiotensin II receptor antagonists in general, would improve aspects of an individual's skin tone, treat

skin aging, or treat wrinkles. Moreover, the instant specification specifically states that the "ACE and angiotensin II are known to be involved in triggering collagen synthesis, whereas teaching with the prior art suggest that aging skin is associated with the reduction collagen" and states that it is surprising and unexpected that the inhibitors and antagonists of said enzymes do not lead to damaging levels of skin collagen production but improve and/or maintain the skin tone of an individual (see page 5 of the instant specification, lines 5-16). Thus, the state of the prior art at the time of the instant invention is that ACE inhibitors and angiotensin II antagonists were not known to improve aspects of an individual's skin tone, treat skin aging, or treat wrinkles.

(4) The amount of direction provided by the inventor: There is nothing in the specification that would indicate that the current invention is able to improve aspects of an individual's skin tone, treat skin aging, or treat wrinkles with each and every ACE inhibitor and/or angiotensin II antagonist. A list of numerous examples of ACE inhibitors and angiotensin II antagonists are provided on page 5, lines 26 to page 8, line 21 of the instant specification. General guidance for the dosage, administration, and formulation of cosmetic formulations, including acceptable cosmetic auxiliaries is provided on page 8, line 24 to page 33, line 20 of the instant specification.

(5) Predictability of the art: The prior art does not teach that each and every ACE inhibitor and/or angiotensin II receptor antagonist will improve aspects of an individual's skin tone, treat skin aging, or treat wrinkles. Although captopril and ACE enzyme inhibitor dipeptides are known to treat some aspects of skin aging, the instant specification states that it expected that ACE inhibitor and/or angiotensin II receptor

antagonist would decrease skin collagen, wherein skin aging is already associated with a reduction in skin collagen. Thus, there is little predictability in the art regarding the improvement of aspects of an individual's skin tone, the treatment of skin aging, or the treatment of wrinkles with each and every ACE inhibitor and/or angiotensin II receptor antagonist.

(6) The presence or absence of working examples: Applicant describes a formulation example of pages 34-36 of the instant specification and prophetic example for the topical application of ACE inhibitors on pages 36-38. However, the Applicant does not supply any concrete evidence that topical application of each and every ACE inhibitor and/or angiotensin II receptor antagonist will improve aspects of an individual's skin tone, treat skin aging, or treat wrinkles.

Overall, applicant fails to provide examples indicating that the instant method can improve aspects of an individual's skin tone, treat skin aging, or treat wrinkles. Therefore, the practitioner would turn to trial and error experimentation to make/use the instant compositions for improving aspects of an individual's skin tone, treating skin aging, or treating wrinkles, without guidance from the specification or the prior art.

(7) The quantity of experimentation: In order to utilize the methods as claimed, the skilled artisan would be presented with an unpredictable amount of experimentation to determine, for example, which ACE inhibitors and/or angiotensin II receptor antagonists were effective in improving aspects of an individual's skin tone, treating skin aging, or treating wrinkles, and effective dosages for each treatment. The number of ACE inhibitors and/or angiotensin II receptor antagonists is extensive. Consequently, a

burdensome amount of research would be required by one of ordinary skill in the art to practice the methods as instantly claimed.

(8) The relative skill of those in the art: The skill of one of ordinary skill in the art is relatively high, i.e., Ph.D. and M.D. level technology.

In the instant case, an impermissible burden of undue experimentation is necessary to determine which ACE inhibitors and/or angiotensin II receptor antagonists are effective in improving aspects of an individual's skin tone, treating skin aging, or treating wrinkles. An exhaustive study would have to be conducted for each inhibitor and/or antagonist, possibly several more times with each study under slightly different conditions. *Genetech,* 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for a search, but compensation for a successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not vague intimations of general ideas that may or may not be workable."

For the above reasons and analysis of the undue experimentation factors, a person skilled in the art would have to engage in undue experimentation to practice the methods of the instant claims with no assurance of success.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-4, 12-16, and 18 rejected under 35 U.S.C. 102(b) as being anticipated by Alert et al. (US 5,728,373 – cited on IDS).

Alert et al. teach cosmetic and dermatologic light protection formulations containing thiols and/or thiol derivatives wherein a preferred thiol is captopril (see abstract; column 3, lines 30-39) and wherein the formulations are suitable for the treatment of UV-induced skin damage (see column 2, lines 43-47). Alert et al. further teach a method for protecting the skin from UVA and UVB radiation comprising applying an adequate of the cosmetic or dermatological formulation to the skin, i.e. topical administration as claimed in the instant claims 1 and 18 (see column 10, lines 1-7). Alert et al. teach the cosmetic formulations can comprise cosmetic auxiliaries (i.e. carrier components) that are usually found in said formulations as claimed in the instant claim 12, and can be formulation into a lotion as claimed in the instant claim 13 (see column 6, line 53 to column 7, line 14).

In regards to claim 14, "repeatedly performing said contacting over an extended period of time" is broadly interpreted as applying a composition without rinsing it off. Thus, the application of the composition as taught by Alert et al. without rinsing the composition is considered to be application for an extended period of time.

In regards to claim 16, skin with UV-induced damage is considered to be skin wherein the aging or wrinkling considered premature.

7. Claims 1-5, 11-16, 18, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Linter (US 2005/0142092 A1 – cited on IDS).

Linter teaches novel cosmetic or dermopharmaceutical compositions for topical use which are used to treat the visible signs of ageing and fatigue such as bags and circles under the eyes, wherein said composition comprises ACE enzyme inhibitor dipeptides (see abstract). The dipeptides can contain the amino acid residues Val, His, Trp, Arg, Tyr, and Phe, and thus are non-thiol containing ACE inhibitors as claimed in the instant claim 5 (see page 2, section [0026]). In an Example, the dipeptide is present in 0.005 g/100g or 50 mg/kg a claimed in the instant claims 11 and 20 (see page 5, Example 1, section [0068]). The compositions consist of cosmetic carriers and cosmetic adjuvants as claimed in the instant claim 12 (see pages 3-4, sections [0050]-[0065]). Suitable composition forms include lotions and creams as claimed in the instant claim 13 (see page 3, column [0046]). Linter further teaches applying the compositions in an a sufficient and effective quantity to the parts of the face in question over a period of time ranging from 2 weeks to 2 months or longer, meeting the limitation of contacting with the skin over an extended period of time as claimed in the instant claim 14 (see pages 2-3, section [0032]). Lintner also teaches that excessive smoking contribute to the appearance of "bags" under the eyes (see page 1, section [0009]).

Smoking induced “bags” is considered to be premature skin ageing as claimed in the instant claim 16.

8. Claims 1-7, 9, 12, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al. (US 6,805,878 B2 – cited on IDS).

Li et al. teach a dermal composition comprising enalapril ethyl ester or another prodrug corresponding to a pharmaceutically active form of an ACE inhibitor (see abstract). Enalalpril ethyl ester is a non-thiol containing, lipophilic ACE inhibitor as claimed in instant claims 5-6. Li et al. further teach other suitable ACE inhibitors include ramipril or lisinopril as claimed in the instant claims 7 and 9 (see column 2, lines 51-56). The ACE inhibitors are in admixture with a carrier as claimed in the instant claim 12 (see column 3, lines 1-2). Li et al. further teach a method of treating a human or animal in need of an ACE inhibitor with a therapeutically effective amount of the drug, that comprising the step of applying the dermal composition containing the ACE inhibitor to the skin, and maintaining the dermal composition in contact with the skin for a predetermined length of time sufficient to administer a therapeutically amount of the drug, i.e. administration over an extended period of time as claimed in the instant claim 14 (see column 3, lines 46-54).

While Li et al. do not explicitly teach applying the composition improves aspects of an individual's skin tone, this is considered to be inherent in the application of the composition since the patient population as instantly claimed includes the patient

population taught by Li et al. It is noted that the patient population as instant claimed in claims 1-14 is not limited.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 11 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alert et al. (US 5,728,373 – cited on IDS) as applied to claims 1-4, 12-16, and 18 above.

Alert et al. is described *supra* as applied to claims 1-4, 12-16, and 18. Alert et al. further teach the thiols or thiol derivatives (i.e. captopril) are preferably present in cosmetic and/or dermatological formulations in 0.01% by weight to 10% by weight (i.e. 100 mg/kg to 100,000 mg/kg), overlapping with the ranges as claimed in the instant claims 11 and 20 (see column 6, lines 26-35).

Alert et al. do not explicitly teach the compositions are applied at least once daily as claimed in the instant claim 19.

It would have been obvious to one of ordinary skill in the art at the time of the invention to apply the compositions for treating UV-induced skin damage to the skin as taught by Alert et al. at least once daily. One of ordinary skill in the art would have been motivated to apply the compositions once daily in order to provide the skin with light protection each day, as the formulations are also protective formulations. One of ordinary skill in the art would have had a reasonable expectation of success in applying the compositions at least once daily because Alert et al. teach a method for protecting the skin from UVA and UVB radiation by applying an adequate amount of the formulation.

In regards to claims 11 and 20, where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. In re

Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

11. Claims 10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linter (US 2005/0142092 A1 – cited on IDS) as applied to claims 1-5, 11-16, 18, and 20 above.

Linter is described *supra* as applied to claims 1-5, 11-16, 18, and 20.

Linter does not explicitly teach a composition comprising at least two ACE inhibitors and/or angiotensin II receptor antagonists as claimed in the instant claim 10. Linter does not explicitly teach the compositions are applied at least once daily as claimed in the instant claim 19.

It would have been obvious to one of ordinary skill in the art at the time of the invention to utilized at least two ACE enzyme inhibitor dipeptides in the composition for treating the visible signs of aging as taught by Lintner. One of ordinary skill in the art would have been motivated to use at least two ACE enzyme inhibitor dipeptides because multiple dipeptides are known in the prior art as ACE enzyme inhibitors. One of ordinary skill in the art would have had a reasonable expectation of success in combining the dipeptides because Lintner teaches multiple dipeptides suitable for treating the visible signs of aging. It is obvious to combine individual compositions

taught to have the same utility to form a new composition for the very same purpose *In re Kerkhoven*, 626 F.2d 846, 205, U.S.P.Q. 1069 (C.C.P.A. 1980).

It would have been obvious to one of ordinary skill in the art at the time of the invention to apply the compositions for treating the visible signs of ageing as taught by Lintner at least once daily. One of ordinary skill in the art would have been motivated to apply the compositions in a sufficient and effective amount to treat the visible signs of ageing. One of ordinary skill in the art would have had a reasonable expectation of success in applying the compositions at least once daily because Lintner teaches applying the compositions in a sufficient and effective quantity over a period of time ranging from two weeks to 2 months or longer, without specifying the compositions are applied on alternating days, or other variable dosing regimens, etc. that would not lead to at least once daily application of the composition.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jody L. Karol whose telephone number is (571)270-3283. The examiner can normally be reached on 8:30 am - 5:00 pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

JLK

/Yong S. Chong/
Primary Examiner, Art Unit 1627